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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/980,881	03/28/2002	Akira Matsumoto	082371-000000US	1327

7590 03/10/2004

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EXAMINER	
SWOPE, SHERIDAN	

ART UNIT	PAPER NUMBER
1652	17

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/980,881	MATSUMOTO, AKIRA	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-7,9,11,16,18-20,24-26,32 and 34-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *3-6,16,18,24-26 and 34-36* is/are allowed.

6)☒ Claim(s) *7,9,11,32,37 and 38* is/are rejected.

7)☒ Claim(s) *19,20 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's Request for Continuing Examination, received October 8, 2003, is acknowledged. It is acknowledged that Claims 1, 2, 8, 10, 12-15, 17, 21-23, 27-31, and 33, are cancelled. It is also acknowledged that Claims 16 and 19 have been amended and new Claims 37 and 38, which are encompassed by the elected invention, have been added. Claims 3-7, 9, 11, 16, 18-20, 24-26, 32, and 34-38 are pending and are hereby examined on their merits.

Claims-Objections

Claims 19, 20, and 26 are objected to.

Claim 19 is objected to for being redundant with Claim 35. It is suggested that the phrase "A drug" in Claim 29 be replaced with "A pharmaceutical composition" and "the drug" be replaced with "the composition". Accordingly, Claim 20 should be amended to recite "The pharmaceutical composition of claim 19...".

Claim 26 is objected to for having a non-defined abbreviation "APP". Said abbreviation should be defined at its first appearance.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 32, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claims 9 and 32, the phrase "wherein said protein comprises the C-terminal 14 amino acids of SEQ ID NO: 9" is indefinite because SEQ ID NO: 9 is only 14 amino acid residues long.

For purposes of examination, it is assumed that the recited protein has, as its C-terminal 14 amino acids, SEQ ID NO: 9. Correction is required and it is suggested said phrase be amended to "wherein said protein comprises, as the C-terminal 14 amino acids, SEQ ID NO: 9".

Claim 37 is indefinite in reciting "An isolated peptide comprising at least 7 amino acids of SEQ ID NO: 9". As written, Claim 37 reads on any protein that has any 7 amino acids selected from the group consisting of Ser, Asn, Pro, Val, Glu, Lys, and Leu, which essentially encompasses any protein. Correction is required. For purposes of examination, it is assumed that Claim 37 is meant to recite an isolated protein comprising the peptide motif of SEQ ID NO: 9 wherein, within said motif, at least 7 amino acids of SEQ ID NO: 9 are conserved.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In this regard, the application disclosure and claims are compared per the factors indicating in the decision re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art.

Each factor is here addressed on the basis of comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 7, 11, 37, and 38 are rejected under 35 U.S.C. 112, first paragraph because, while the specification is enabling for the polypeptides of SEQ ID NO: 2-4, production of the recombinant polypeptides of SEQ ID NO: 2-4, using the polypeptides of SEQ ID NO: 2-4, or fragments thereof, in a binding assay, and a peptide consisting of SEQ ID NO: 9, the specification does not reasonably provide enablement for (i) any polypeptide comprising the motif of SEQ ID NO: 9 wherein, within said motif, at least 7 amino acids of SEQ ID NO: 9 are conserved, (ii) production of any recombinant protein, (iii) using fragments of any variant of SEQ ID NO: 2-4 in a binding assay, or (iv) any peptide variant of SEQ ID NO: 9 in which no more than 5 residues have been altered, added and/or deleted. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 7 is so broad as to encompass the production of any recombinant protein. Claim 11 is so broad as to encompass using fragments of any variant of SEQ ID NO: 2-4 in a binding assay. Claim 37 is so broad as to encompass any polypeptide comprising the motif of SEQ ID NO: 9 wherein, within said motif, at least 7 amino acids of SEQ ID NO: 9 are conserved. Claim 38 is so broad as to encompass any peptide variant of SEQ ID NO: 9 in which no more than 5 residues have been altered, deleted, and/or added. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be

tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the polypeptides of SEQ ID NO: 2-4.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claims 7, 11, 37, and 38 which, encompass (i) production of any recombinant protein, (ii) a binding assay using fragments of any variant of SEQ ID NO: 2-4, (iii) any protein comprising SEQ ID NO: 9 wherein at least 7 residues of SEQ ID NO: 9 are conserved, and (iv) a peptide variant of SEQ ID NO: 9 wherein no more than 5 amino acids are altered.

The specification does not support the broad scope of Claim 7 because the specification does not establish: (A) the structure or activity of any recombinant protein expressed; (B) regions of any said protein's structure which may be modified without effecting the activity of said protein; (C) the general tolerance of the activity of said proteins to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an

expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices of recombinant proteins is likely to be successful.

The specification does not support the broad scope of Claim 11 because the specification does not establish: (A) the activity of any fragment of any variant of SEQ ID NO: 2-4 in a binding assay; (B) regions of any fragment of SEQ ID NO: 2-4 which may be modified without effecting the activity of said fragment in a binding assay to identify agents that bind to SEQ ID NO: 2-4; (C) the general tolerance of the binding activity of any fragments of SEQ ID NO: 2-4 to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues of fragments of SEQ ID NO: 2-4 with an expectation of obtaining the desired binding activity; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices of variant fragments is likely to be successful in identifying compounds that bind to SEQ ID NO: 2-4.

The specification does not support the broad scope of Claim 37 because the specification does not establish: (A) the activity of any protein comprising the motif of SEQ ID NO: 9 wherein, within said motif, at least 7 residues of SEQ ID NO: 9 are conserved; (B) regions of any said protein's structure which may be modified without effecting the activity of said protein; (C) the general tolerance of the activity of said protein to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices of proteins is likely to be successful.

The specification does not support the broad scope of Claim 38 because the specification does not establish: (A) the activity of any peptide variant of SEQ ID NO: 9 in which no more than 5 residues have been altered, deleted, and/or added; (B) regions of any said peptide's structure which may be modified without effecting the activity of said peptide; (C) the general tolerance of the activity of said peptide to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including (i) any polypeptide comprising the motif of SEQ ID NO: 9 wherein, within said motif, at least 7 amino acids of SEQ ID NO: 9 are conserved, (ii) production of any recombinant protein, (iii) using fragments of any variant of SEQ ID NO: 2-4 in a binding assay, or (iv) any peptide variant of SEQ ID NO: 9 in which no more than 5 residues have been altered, added, and/or deleted. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 7, 11, 37, and 38 are rejected under 35 U.S.C. 112, first paragraph, for insufficient functional written description, while Claims 7, 11, and 37 are rejected under 35 U.S.C. 112, first

paragraph, for insufficient structural written description. Claims 7, 11, 37, and 38 contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 7 is directed to a method for producing a genus of recombinant proteins. The specification does not contain any disclosure of the function of all said recombinant proteins. The genus of proteins that comprise these above recombinant molecules is a large variable genus with the potentiality of being many different proteins. Therefore, many functionally unrelated recombinant proteins are encompassed within the scope of these claims, including partial polypeptides, and polypeptides with no function. The specification discloses the function of only a three species of the claimed genus, the carboxypeptidases set forth by SEQ ID NO: 2-4, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. In addition, the specification teaches the structure of only three single representative species of such proteins, SEQ ID NO: 2-4, and the specification fails to describe any other representative species by any identifying structural characteristics or properties. Given this lack of functional and structural description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim 11 is directed to a method of using a genus of peptide fragments of any variant of SEQ ID NO: 2-4 in a binding assay. The specification does not contain any disclosure of the function of all said peptide fragments in a binding assay. The genus of fragments that comprise

these above peptides is a large variable genus with the potentiality of being many different peptides. Therefore, many functionally unrelated peptides are encompassed within the scope of these claims. The specification discloses the function of no species of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. In addition, the specification teaches the structure of no representative species of such fragments. Given this lack of functional and structural description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim 37 is directed to genus of proteins comprising any polypeptide comprising the motif of SEQ ID NO: 9 wherein, within said motif, at least 7 amino acids of SEQ ID NO: 9 are conserved. The specification does not contain any disclosure of the function of all said proteins. The genus of proteins that comprise these above polypeptides is a large variable genus with the potentiality of being many different proteins. Therefore, many functionally unrelated proteins are encompassed within the scope of these claims. The specification discloses the function of only three species of the claimed genus, the carboxypeptidases of SEQ ID NO: 2-4, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. In addition, the specification teaches the structure of only three representative species of such proteins, SEQ ID NO: 2-4, and the specification fails to describe any other representative species by any identifying structural characteristics or properties, other than comprising the motif of SEQ ID NO: 9 wherein, within said motif, at least 7 amino acids of SEQ ID NO: 9 are conserved. Given this lack of functional and structural description of

representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim 38 is directed to genus of peptides comprising any variant of SEQ ID NO: 9 in which no more than 5 residues have been altered, deleted, and/or added. The specification does not contain any disclosure of the function of all said peptides. The genus of peptides that comprise these above variants is a large variable genus with the potentiality of being many different peptides. Therefore, many functionally unrelated peptides are encompassed within the scope of these claims, including peptides with no function. The specification discloses the function of no species of the claimed genus. Given this lack of functional description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Fenselau et al, 1996 or Napier et al, 1992. Fenselau et al teach a polypeptide comprising the motif of SEQ ID NO: 9, wherein, within said motif, 10 amino acid residues of SEQ ID NO: 9 are conserved. Napier et al teach a polypeptide comprising the motif of SEQ ID NO: 9, wherein, within said motif, 9 amino acid residues of SEQ ID NO: 9 are conserved. Therefore, Claim 37 is rejected under 35 U.S.C. 102(b) as being anticipated by Fenselau et al, 1996 or Napier et al, 1992.

Allowable Subject Matter

Claims 3-6, 16, 18, 24-26, and 34-36 are allowable.

Claims 19 and 29 are objected to, but would be allowable if rewritten to address the indicated objections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan Lee Swope, Ph.D.

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